Complete Summary

GUIDELINE TITLE

2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension.

BIBLIOGRAPHIC SOURCE(S)

2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003 Jun;21(6):1011-53. [342 references] PubMed

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SCOPE

DISEASE/CONDITION(S)

Hypertension

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To offer the best available and most balanced information to all those involved in the management of arterial hypertension
- To provide guidelines that have been prepared on the basis of the best available evidence on all issues deserving recommendations, and with the consideration that guidelines should have an educational purpose more than a prescriptive one

TARGET POPULATION

Patients with hypertension

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Repeated blood pressure measurements
2. Medical history
3. Physical examination for evidence of additional risk factors (in particular abdominal obesity), for signs suggesting secondary hypertension, and for evidence of organ damage.
4. Laboratory and instrumental investigations
5. Electrocardiography
6. Ultrasound examination of carotid arteries
7. Echocardiography
8. Signs and symptoms
9. Kidney function tests
10. Blood chemistry
11. Haemoglobin and haematocrit
12. Urinalysis
13. Funduscopy
14. Magnetic resonance imaging
15. Computed tomography

Treatment

1. Lifestyle changes including smoking cessation, weight reduction, reduction of excessive alcohol intake, physical exercise, reduction of salt intake, and increase in fruit and vegetable intake and decrease in saturated and total fat intake
2. Calcium antagonists (amlodipine, verapamil, nifedipine, lacidipine, isradipine)
3. Angiotensin-converting enzyme inhibitors (lisinopril, trandolapril, enalapril, fosinopril, ramipril)
4. Diuretics (chlorthalidone, hydrochlorothiazide)
5. Beta blockers (atenolol)
6. Angiotensin II antagonist (candesartan, losartan, irbesartan)

7. Alpha-blockers (doxazosin)
8. Sympatholytic agents (atenolol, clonidine and/or reserpine)
9. Monotherapy versus combination therapy

MAJOR OUTCOMES CONSIDERED

- Total cardiovascular risk
- Cardiovascular morbidity and mortality
- All-cause morbidity and mortality
- Risk of fatal and non-fatal events
- Left ventricular hypertrophy
- Presence of atherosclerosis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The members of the Guidelines Committee, established by the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC,) have participated independently in the preparation of this document, drawing on their academic and clinical experience and utilizing an objective and critical examination of all available literature.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The following is a brief statement of the practice recommendations for the management of hypertension. The reader should refer to the original guideline document for detailed management recommendations and a critical assessment of the evidence for the recommendations.

Procedures for blood pressure measurement

When measuring blood pressure, care should be taken to:

- Allow the patients to sit for several minutes in a quiet room before beginning blood pressure measurements.
- Take at least two measurements spaced by 1 to 2 minutes, and additional measurements if the first two are quite different.
- Use a standard bladder (12–13 cm long and 35 cm wide) but have a larger and a smaller bladder available for fat and thin arms, respectively. Use the smaller bladder in children.
- Have the cuff at the heart level, whatever the position of the patient.
- Use phase I and V (disappearance) Korotkoff sounds to identify systolic and diastolic blood pressure, respectively.

- Measure blood pressure in both arms at first visit to detect possible differences due to peripheral vascular disease. In this instance, take the higher value as the reference one, when the auscultatory method is employed.
- Measure blood pressure 1 and 5 minutes after assumption of the standing position in elderly subjects, diabetic patients, and in other conditions in which orthostatic hypotension may be frequent or suspected.
- Measure heart rate by pulse palpation (30 s) after the second measurement in the sitting position.

Blood pressure measurement

- Blood pressure values measured in the doctor´s office or the clinic should commonly be used as reference.
- Twenty-four-hour ambulatory blood pressure monitoring may be considered of additional clinical value, when:
    - Considerable variability of office blood pressure is found over the same or different visits.
    - High office blood pressure is measured in subjects otherwise at low global cardiovascular risk.
    - There is marked discrepancy between blood pressure values measured in the office and at home.
    - Resistance to drug treatment is suspected.
    - Research is involved.
- Self-measurement of blood pressure at home should be encouraged in order to:
    - Provide more information for the doctor´s decision
    - Improve patient´s adherence to treatment regimens
- Self-measurement of blood pressure at home should be discouraged whenever:
    - It causes patients anxiety.
    - It induces self-modification of the treatment regimen.
- Normal values are different for office, ambulatory, and home blood pressure

Guidelines for family and clinical history

- Duration and previous level of high blood pressure
- Indications of secondary hypertension
    - Family history of renal disease (polycystic kidney)
    - Renal disease, urinary tract infection, haematuria, analgesic abuse (parenchymal renal disease)
    - Drug/substance intake: oral contraceptives, liquorice, carbenoxolone, nasal drops, cocaine, amphetamines, steroids, non-steroidal anti-inflammatory drugs, erythropoietin, cyclosporin
    - Episodes of sweating, headache, anxiety, palpitation (phaeochromocytoma);
    - Episodes of muscle weakness and tetany (aldosteronism).
- Risk factors
    - Family and personal history of hypertension and cardiovascular disease
    - Family and personal history of hyperlipidaemia
    - Family and personal history of diabetes mellitus
    - Smoking habits

    - Dietary habits
    - Obesity; amount of physical exercise
    - Personality
- Symptoms of organ damage
    - Brain and eyes: headache, vertigo, impaired vision, transient ischaemic attacks, sensory or motor deficit
    - Heart: palpitation, chest pain, shortness of breath, swollen ankles
    - Kidney: thirst, polyuria, nocturia, haematuria
    - Peripheral arteries: cold extremities, intermittent claudication
- Previous antihypertensive therapy
    - Drugs used, efficacy and adverse effects
- Personal, family, and environmental factors

Physical examination for secondary hypertension and organ damage

Signs suggesting secondary hypertension and organ damage

- Features of Cushing syndrome
- Skin stigmata of neurofibromatosis (phaeochromocytoma)
- Palpation of enlarged kidneys (polycystic kidney)
- Auscultation of abdominal murmurs (renovascular hypertension)
- Auscultation of precordial or chest murmurs (aortic coarctation or aortic disease)
- Diminished and delayed femoral and reduced femoral blood pressure (aortic coarctation, aortic disease)

Signs of organ damage

- Brain: murmurs over neck arteries, motor or sensory defects
- Retina: funduscopic abnormalities
- Heart: location and characteristics of apical impulse, abnormal cardiac rhythms, ventricular gallop, pulmonary rales, dependent oedema
- Peripheral arteries: absence, reduction, or asymmetry of pulses, cold extremities, ischaemic skin lesions

Laboratory investigations

Routine tests

- Plasma glucose (preferably fasting)
- Serum total cholesterol
- Serum high-density lipoprotein (HDL)-cholesterol
- Fasting serum triglycerides
- Serum uric acid
- Serum creatinine
- Serum potassium
- Haemoglobin and haematocrit
- Urinalysis (dipstick test complemented by urinary sediment examination)
- Electrocardiogram

Recommended tests

- Echocardiogram
- Carotid (and femoral) ultrasound
- C-reactive protein
- Microalbuminuria (essential test in diabetics)
- Quantitative proteinuria (if dipstick test positive)
- Funduscopy (in severe hypertension)

Extended evaluation (domain of the specialist)

- Complicated hypertension: tests of cerebral, cardiac, and renal function
- Search for secondary hypertension: measurement of renin, aldosterone, corticosteroids, catecholamines; arteriography; renal and adrenal ultrasound; computer-assisted tomography (CAT); brain magnetic resonance imaging

Goals of treatment

- The primary goal of treatment of the patient with high blood pressure is to achieve the maximum reduction in the long-term total risk of cardiovascular morbidity and mortality. This requires treatment of all the reversible risk factors identified, including smoking, dyslipidaemia, or diabetes, and the appropriate management of associated clinical conditions, as well as treatment of the raised blood pressure per se.
- On the basis of current evidence from trials, it can be recommended that blood pressure, both systolic and diastolic, be intensively lowered at least below 140/90 mmHg and to definitely lower values, if tolerated, in all hypertensive patients, and below 130/80 mmHg in diabetics, keeping in mind, however, that systolic values below 140 mmHg may be difficult to achieve, particularly in the elderly.

Lifestyle changes

- Lifestyle measures should be instituted whenever appropriate in all patients, including subjects with high normal blood pressure and patients who require drug treatment. The purpose is to lower blood pressure and to control other risk factors and clinical conditions present.
- The lifestyle measures that are widely agreed to lower blood pressure or cardiovascular risk and that should be considered, are:
    - Smoking cessation
    - Weight reduction
    - Reduction of excessive alcohol intake
    - Physical exercise
    - Reduction of salt intake
    - Increase in fruit and vegetable intake and decrease in saturated and total fat intake

Monotherapy versus combination therapy

- In most, if not all, hypertensive patients, therapy should be started gradually and target blood pressure values achieved progressively through several weeks.
- To reach target blood pressure, it is likely that a large proportion of patients will require combination therapy with more than one agent.

- According to the baseline blood pressure and the presence or absence of complications, it appears reasonable to initiate therapy either with a low dose of a single agent or with a low-dose combination of two agents.
- There are advantages and disadvantages with either approach.

Choice of antihypertensive drugs

- The main benefits of antihypertensive therapy are due to lowering of blood pressure per se.
- There is also evidence that specific drug classes may differ in some effect or in special groups of patients.
- Drugs are not equal in terms of adverse disturbances, particularly in individual patients.
- The major classes of antihypertensive agents – diuretics, beta blockers, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor antagonists – are suitable for the initiation and maintenance of therapy.
- Emphasis on identifying the first class of drugs to be used is probably outdated by the need to use two or more drugs in combination in order to achieve goal blood pressure.
- Within the array of available evidence, the choice of drugs will be influenced by many factors, including:
    - Previous experience of the patient with antihypertensive agents
    - Cost of drugs
    - Risk profile, presence or absence of target organ damage, clinical cardiovascular or renal disease or diabetes
    - Patient´s preference

Antihypertensive therapy in the elderly

- There is little doubt from randomized controlled trials that older patients with systolic–diastolic or with isolated systolic hypertension benefit from antihypertensive treatment in terms of reduced cardiovascular morbidity and mortality.
- Initiation of antihypertensive treatment in elderly patients should follow the general guidelines but should be particularly gradual, especially in frail individuals.
- Blood pressure measurement should also be performed in the erect posture, to exclude patients with marked postural hypotension from treatment and to evaluate postural effects of treatment.
- Many elderly patients will have other risk factors, target organ damage, and associated cardiovascular conditions, to which the choice of the first drug should be tailored.
- Many elderly patients need two or more drugs to control blood pressure, particularly since it is often difficult to lower systolic blood pressure to below 140 mmHg.
- In subjects aged 80 years and over, a recent meta-analysis concluded that fatal and nonfatal cardiovascular events, but not mortality, are reduced by antihypertensive therapy.

Antihypertensive therapy in diabetics

- Non-pharmacological measures (particularly weight loss and reduction in salt intake) should be encouraged in all patients with type 2 diabetes, independently of the existing blood pressure. These measures may suffice to normalize blood pressure in patients with high normal or grade 1 hypertension and can be expected to facilitate blood pressure control by antihypertensive agents.
- The goal blood pressure to aim at during behavioural or pharmacological therapy is below 130/80 mmHg.
- To reach this goal, most often combination therapy will be required.
- It is recommended that all effective and well-tolerated antihypertensive agents are used, generally in combination.
- Available evidence indicates that renoprotection benefits from the regular inclusion in these combinations of an ACE inhibitor in type 1 diabetes and of an angiotensin receptor antagonist in type 2 diabetes.
- In type 2 diabetic patients with high normal blood pressure, who may sometimes achieve blood pressure goal by monotherapy, the first drug to be tested should be a blocker of the renin–angiotensin system.
- The finding of microalbuminuria in type 1 or 2 diabetics is an indication for antihypertensive treatment, especially by a blocker of the renin–angiotensin system, irrespective of the blood pressure values.

Antihypertensive therapy in patients with deranged renal function

- Before antihypertensive treatment became available, renal involvement was frequent in patients with essential hypertension.
- Renal protection in diabetes has two main requirements:
    - Strict blood pressure control (<130/80 mmHg and even lower if proteinuria is >1 g/day)
    - Lowering proteinuria to values as near to normal as possible.
- To reduce proteinuria either an angiotensin receptor blocker or an ACE inhibitor is required.
- To achieve the blood pressure goal, combination therapy is usually required, with addition of a diuretic and a calcium antagonist.
- To prevent or retard nephrosclerosis in hypertensive nondiabetic patients, blockade of the renin–angiotensin system appears more important than attaining very low blood pressure, but evidence is so far restricted to African-American hypertensives, and suitable studies in other ethnic groups are required. It appears prudent, however, to lower blood pressure intensively in all hypertensive patients with deranged renal function.
- An integrated therapeutic intervention (antihypertensives, statins, antiplatelet therapy, etc.) frequently has to be considered in patients with renal damage.

Causes of resistant hypertension

- Unsuspected secondary cause
- Poor adherence to therapeutic plan
- Continued intake of drugs that raise blood pressure
- Failure to modify lifestyle including:
    - Weight gain
    - Heavy alcohol intake (i.e., binge drinking)
- Volume overload due to:
    - Inadequate diuretic therapy

- Progressive renal insufficiency
- High sodium intake

Causes of spurious resistant hypertension

- Isolated office (white-coat) hypertension
- Failure to use large cuff on large arm

Treatment of associated risk factors

Lipid-lowering agents

- All patients up to the age of 80 with active coronary heart disease, peripheral arterial disease, history of ischaemia, stroke, and long-standing type 2 diabetes should receive a statin if their total cholesterol is >3.5 mmol/l (135 mg/dl), with the goal of reducing it by about 30%.
- Patients without overt cardiovascular disease or with recent-onset diabetes, whose estimated 10-year cardiovascular risk is $\geq$20% ("high" risk in Table 2 in the original guideline document), should also receive a statin if their total cholesterol is >3.5 mmol/l (135 mg/dl).

Antiplatelet therapy

- Antiplatelet therapy, in particular low-dose aspirin, should be prescribed to patients with previous cardiovascular events, as it has been shown to reduce the risk of stroke and myocardial infarction (provided patients are not at an excessive risk of bleeding).
- In hypertensive patients, low-dose aspirin has been shown to be beneficial (reduction of myocardial infarction greater than the risk of excess bleeding) in patients older than 50 with an even moderate increase in serum creatinine, or with a 10-year total cardiovascular risk $\geq$20% ("high" risk in Table 2 in the original guideline document).
- In hypertensives, low-dose aspirin administration should be preceded by good blood pressure control.

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for the initiation of antihypertensive treatment and for choosing between monotherapy and combination therapy.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Although large randomized controlled trials and their meta-analyses provide the strongest evidence about several aspects of therapy, scientific evidence is drawn from many sources and, where necessary, all sources have been used.

These recommendations have been accompanied by relevant references, and those articles based on large randomized trials, meta-analyses, or large observational studies have been clearly identified in the original guideline document.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

With the preparation of these guidelines, the European Society of Hypertension and the European Society of Cardiology respond to the suggestion of the World Health Organization/International Society of Hypertension guidelines that regional experts draw up recommendations specifically directed toward the management of patients in their own region.

POTENTIAL HARMS

Particular attention should be given to adverse events, even purely subjective disturbances, because they may be an important cause of noncompliance. The patients should always be asked about adverse effects, and dose or drug changes made accordingly. Some adverse effects have a similar incidence for all compounds of the same class (e.g., cough for angiotensin-converting enzyme inhibitors), whereas for other adverse events there may be compounds within the same drug class less prone to induce them (e.g., among beta blockers less fatigue or Raynaud´s phenomenon with vasodilating compounds; among calcium antagonists no constipation with dihydropyridines, no tachycardia with verapamil and diltiazem).

CONTRAINDICATIONS

CONTRAINDICATIONS

- Thiazide diuretics are contraindicated in patients with gout (compelling) and in pregnant patients (possible).
- Anti-aldosterone diuretics are contraindicated in patients with renal failure or hyperkalaemia (compelling).
- Beta blockers are contraindicated in patients with asthma, chronic obstructive pulmonary disease, or grade 2 or 3 atrioventricular block (compelling) and in patients with peripheral vascular disease or glucose intolerance and in athletes and physically active patients (possible).
- Dihydropyridine calcium antagonists are contraindicated in patients with tachyarrhythmias or congestive heart failure (possible).
- The calcium antagonists verapamil and diltiazem are contraindicated in patients with grade 2 or 3 atrioventricular block or congestive heart failure (compelling).
- Angiotensin-converting enzyme inhibitors are contraindicated in pregnancy and in patients with hyperkalaemia or bilateral renal artery stenosis (compelling).
- Angiotensin II receptor antagonists are contraindicated in pregnancy and in patients with hyperkalaemia or bilateral renal artery stenosis (compelling).

- Alpha-blockers are contraindicated in patients with orthostatic hypotension (compelling) and in patients with congestive heart failure (possible).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The Committee is aware that it is easier to prepare guidelines on a medical condition in general than to deal with the individual patients with that condition requiring medical advice and intervention. Because of this awareness, the Committee has tried to avoid giving rigid rules that would constrain judgement on the management of individual patients differing in their personal, medical and cultural characteristics.
- These guidelines have been prepared on the basis of the best available evidence for all key recommendations, and with the principle that guidelines should be educational rather than merely prescriptive.
- The Committee members take the view that, although large randomized controlled trials and meta-analyses provide the strongest evidence about several aspects of therapy, scientific evidence is drawn from many sources, and where necessary all sources have been used. Therefore, the Committee has avoided rigid classification of its recommendations dependent upon the strength of available evidence.

Values and limitations of event-based clinical randomized trials

- Values
  - Randomization is the safest procedure to avoid bias.
  - Large number of patients guarantees power to detect differences in primary endpoint.
  - Most events used as endpoints are well-defined events of clinical relevance.
- Limitations
  - Selection of patients (most often patients at elevated cardiovascular risk): extrapolation to patients at a different risk level is doubtful.
  - Most trials are not powered for secondary endpoints.
  - Therapeutic programmes in trials often diverge from those followed in clinical practice.
  - Compliance of patients in trials is much higher than in clinical practice.
  - Controlled randomized trials last for 4 to 5 years, whereas life expectation in middle-aged hypertensives is of 20 to 30 years.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Despite major efforts to diagnose and to treat hypertension, this condition remains worldwide a leading cause of cardiovascular morbidity and mortality, and goal blood pressure levels are seldom achieved. It is therefore highly desirable to improve this unsatisfactory delivery of care. In the field of hypertension, an increasing number of clinical trials allow the formulation of guidelines to support a more effective strategy. The availability of guidelines should not only help

clinicians to take decisions in everyday practice, but also make the health authorities in all countries aware of the critical points to consider in order to improve hypertension management. The experience accumulated so far suggests that the impact of guidelines in changing clinical practice is rather small. Multifaceted interventions are required to implement guidelines successfully, going from the dissemination of recommendations to educational programmes at the practice site. This requires the participation of all professionals involved in health care, from governmental level to the individual physician. Consequently, broad acceptance of the present guidelines by national hypertension societies and leagues is a prerequisite to promoting behavioural changes in practice and, thereby, improving patient outcomes. In this context, the present guidelines have been prepared in concert with the Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention, in view of their incorporation in the comprehensive guidelines on prevention of cardiovascular diseases in clinical practice these societies are preparing.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003 Jun;21(6):1011-53. [342 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Jun

GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society
European Society of Hypertension - Disease Specific Society

SOURCE(S) OF FUNDING

Expenses for the Writing Committee and preparation of theses guidelines were provided entirely by the European Society of Hypertension.

GUIDELINE COMMITTEE

European Society of Hypertension-European Society of Cardiology Guidelines Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

No member of the Guidelines Committee owns stock of pharmaceutic or biomedical industries except W. Kiowski (Novartis, Pfizer, Roche) and E. O´Brien (minority interest in Medical Management Systems Ltd).

The following members have served as consultants for, received personal compensation from, or were grant recipients of the following industries or government or private health providers during the past 5 years: G. Mancia: Abbott (Knoll), AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmith- Kline, Merck, Novartis, Pfizer, Servier, Solvay, Takeda, Italian

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ENDORSER(S)

International Society of Hypertension

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the European Society of Hypertension Web site.

Print copies: Available from Elsevier Science Ltd. European Heart Journal, ESC Guidelines - Reprints, 32 Jamestown Road, London, NW1 7BY, United Kingdom. Tel: +44.207.424.4422; Fax: +44 207 424 4515; E-mail: gr.davies@elsevier.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Recommendations for Task Force Creation and Report Production. A document for Task Force members and expert panels responsible for the creation and production of Guidelines and Expert Consensus Documents. 2002 Apr.

Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Elsevier Publishers Ltd., 32 Jamestown Road, London, NW1 7BY, United Kingdom. Tel: +44.207.424.4422; Fax: +44 207 424 4433; E-mail: gr.davies@elsevier.com

PATIENT RESOURCES

None available

NGC STATUS

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